REMARKS

In response to the Office Action dated October 2, 2002, claims 34 and 36 have been amended, and new claims 38-43 have been added. No new matter has been added. Support for claims 38, and 40-42 can be found throughout the specification as filed, for example, on page 18, line 11, to page 20, line 10. Support for the new claims 39 and 43 can be found, for example, on page17, lines 25-30. Claims 1-28, and 34-43 are pending in the application. Reconsideration is respectfully requested.

I. Rejection under 35 U.S.C.§ 112 first paragraph

On page 2 of the Office Action, claims 1-28 and 34-37 are rejected under 35 U.S.C. § 112 first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner rejected claims 1-28 as confusing and unclear how the linkers and bridge molecules differ chemically. The Examiner also rejected claims 34-37 as confusing and unclear as to the meaning and scope of "modified tissue" and "modified sites."

Applicants respectfully traverse the rejection.

Claims 1 and 16 recite that the linkers and the bridge molecules are chemically different. Applicants respectfully submit that the phrase "chemically different" is not confusing or unclear. Chemical compounds have chemical and physical properties. "Chemically different" means differences in the chemical properties, which can be structural. They may or may not be different in physical properties including boiling points, melting points, solubility and so on. In any event, the focus is on the chemical differences and the phrase "chemically different" complies with 35 U.S.C.§ 112. Claims 2-15 and 17-28 are dependent from claims 1 and 16, respectively, thus they also comply with 35 U.S.C.§ 112. Applicants respectfully request that the rejection of claims 1-28 under 35 U.S.C.§ 112 first paragraph be withdrawn. Reconsideration is respectfully requested.

Applicants further submit that claims 34-37 are not confusing and unclear as to the meaning of "modified tissue" and "modified sites". When a tissue is modified, it is considered as having a modified site or sites. However, in the interest of furthering the

prosecution, claims 34 and 36 have been amended for clarity. Applicants respectfully submit that the amendments to claims 34-37 do not change the scope of the claims in any manner and that the amended claims comply with 35 U.S.C.§ 112 first paragraph. Applicants respectfully request that the rejection that claims 34-37 under 35 U.S.C.§ 112 first paragraph be withdrawn. Reconsideration is respectfully requested.

II. Rejection under 35 U.S.C. § 103(a)

On page 3 of the Office Action, claims 1-28 and 34-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ogle, et al. (U.S. 5,958,669) in view of Yang, et al. (5,935,168).

Applicants respectfully traverse the rejection.

Ogle, et al. pertains to a method and apparatus for crosslinking a tissue using a semi-permeable member for screening crosslinking compounds not having the desired molecular weight. Col. 1 line 47 to col. 2 line 57. As noted by the Examiner, the tissue is crosslinked with glutaraldehyde. Since crosslinking compounds, such as dialdehydes, can polymerize spontaneously in solution, selection of the oligomers having the required molecular weight can improve the characteristic of the crosslinked tissue. See col. 3, lines 3-7. By the screening method described, polymerization is controlled and the oligomers having the desired molecular weight can crosslink the tissue prior to further polymerization to produce large oligomers. See col. 3, lines 8-12.

Yang, et al. pertains to a tissue crosslinked with glutaraldhyde which is then reacted with a diamine to replace at least some of the carboxyl groups present on the collagen and/or elastin molecules with non-carboxyl side groups. See col. 3, lines 2-17, and Figure 2. This is done because glutaraldhyde fixed tissue is prone to calcification. See col. 3, lines 44-64. There is no bonding of the crosslinkers to each other with bridge molecules, as the crosslinkers are already crosslinked to the tissue. See Figure 2.

On the other hand, claims 1 and 16 disclose a tissue comprising linkers bonded to the tissue and a bridge molecule bonded between two or more of the linkers, and the linkers and bridges are chemically different. Linkers link to the tissue on one end,

and instead of linking to the tissue on its other end, the linkers are linked to bridge molecules that are distinguished chemically from linkers. Linkers can be glutaraldhyde.

While Ogle, et al. and Yang, et al. both teach the use of glutaraldhyde as a crosslinker, Ogle, et al. does not teach a tissue having glutaraldhyde linkers and bridge molecules that are chemically different from glutaraldhyde, to bond such crosslinkers together. This deficiency is not supplied by Yang, et al., as Yang, et al. also teach the same crosslinking with glutaraldhyde. See Figure 2. No bridge molecule, chemically different from the crosslinker, is mentioned or taught in Ogle, et al. or Yang, et al., individually or combined

Claim 34 discloses bridge molecules bonded to two or more modified sites of the tissue. This is also not taught in Ogle, et al. This deficiency is also not supplied by Yang, et al., as noted above. In addition, Yang, et al. teaches that glutaraldhyde can either be used to crosslink the tissue itself, or if amines are used to treat the tissue to minimize calcification, they can be further crosslinked with glutaraldhyde. See Figure 2. These glutaraldehyde compounds are not further bonded to bridge molecules. Therefore, bridge molecules for bonding modified sites of the tissue are not taught.

Three criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or combination of references, must teach or suggest all the claim limitations. MPEP § 2142. Applicants respectfully submit that since Yang, et al. does not supply the deficiency of Ogle, et al., as no bridge molecules, chemically different from linkers, or bridge molecules linking sites in tissues that have been modified, are mentioned or taught in Ogle, et al. or Yang, et al., individually or combined, the prior art fails to disclose all the claim limitations. Additionally, there would be no motivation to combine the references as proposed by the Examiner.

Dependent claims 2-15, 17-28, and 35-37, which are dependent from independent claims 1, 16 and 34, respectively, were also rejected under 35 U.S.C.

§103(a) as being unpatentable over Ogle, et al. (U.S. 5,958,669) in view of Yang, et al. (5,935,168).

While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claims 1, 16 and 34. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 2-15 and 17-28, and 35-37 are also in condition for allowance.

In view of the amendments and reasons provided above, it is believed that all pending claims are in condition for allowance. Applicants respectfully request favorable reconsideration and early allowance of all pending claims.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Attorney for the Applicants, Hallie A. Finucane at 952.253.4134.

Respectfully submitted,

Altera Law Group, LLC

Date: February 3, 2003 By: Hallie A. Finucane

Hallie A. Finucane
Reg. No. 33,172
Direct Dial: 952.253.4134

HAF:mar

Appendix A
Marked Up Version of the Entire Claim Set

The entire set of pending claims is provided for the Examiner's convenience.

1. (Unchanged) A tissue comprising linkers bonded to the tissue and a bridge molecule bonded between two or more of the linkers, wherein the linkers and the bridges are chemically different.

2. (Unchanged) The tissue of claim 1 wherein the tissue comprises extracellular matrix selected from the group consisting of collagenous fibrils, GAG and elastin.

3. (Unchanged) The tissue of claim 1 wherein the two linkers and the bridge bonded between the two linkers span a distance of between about 10 Angstroms and about 100 Angstroms.

4. (Unchanged) The tissue of claim 1 wherein the two linkers and the bridge bonded between the two linkers span a distance of between about 15 Angstroms and about 50 Angstroms.

5. (Unchanged) The tissue of claim 1 wherein the bridge is a single molecule.

6. (Unchanged) The tissue of claim 1 wherein the bridge is reactive with modified tissue.

7. (Unchanged) The tissue of claim 1 wherein the bridge comprises functional groups selected from the group consisting of methylthio, thio, amine, alcohol, carboxyl and combinations thereof.

8. (Unchanged) The tissue of claim 1 wherein the bridge comprises a hydrocarbon backbone.

9. (Unchanged) The tissue of claim 1 wherein the linkers comprise monomers, dimers and oligomers.

10. (Unchanged) The tissue of claim 1 wherein the linkers are active with respect to the tissue.

11. (Unchanged) The tissue of claim 1 wherein the linkers comprise functional groups selected from the group consisting of aldehydes, epoxies, imide groups, photooxidative groups, enzymatically oxidative groups and combinations thereof.

12. (Unchanged) The tissue of claim 1 wherein the linkers comprise crosslinking agents.

13. (Unchanged) The tissue of claim 1 wherein the linker is selected from the group consisting of glutaraldehyde, triglycidyl amine and epoxy.

14. (Unchanged) The tissue of claim 1 wherein a bioprosthetic device comprises the tissue.

15. (Unchanged) The tissue of claim 14 wherein the bioprosthetic device is a heart valve prosthesis.

16. (Unchanged) A method of crosslinking tissue comprising treating the tissue with a linker composition comprising linkers and a bridge composition comprising bridges wherein the linkers bond to the tissue and the bridges bond between two of the linkers, wherein the bridges and the linkers are chemically different.

17. (Unchanged) The method of claim 16 wherein the tissue comprises proteins.

18. (Unchanged) The method of claim 16 wherein the tissue is treated with the linker composition and the bridge composition simultaneously.

19. (Unchanged) The method of claim 16 wherein the tissue is treated with the linker composition prior to addition of the bridge composition.

20. (Unchanged) The method of claim 16 wherein the linker composition and the bridge composition are combined prior to treating the tissue.

21. (Unchanged) The method of claim 16 wherein the linker composition comprises crosslinking agents.

22. (Unchanged) The method of claim 16 wherein the concentration of the linkers in the linker composition is between about 0.0001 molar and about molar.

23. (Unchanged) The method of claim 16 wherein the concentration of the bridges in the bridge composition is between about 1×10^{-7} molar and about 1 molar.

24. (Unchanged) The method of claim 16 wherein the tissue is treated with the linker composition and the bridge composition for between about 10 minutes and about one month.

25. (Unchanged) The method of claim 16 wherein the tissue is treated with the linker composition and the bridge composition for between about 10 minutes and about 2 weeks.

26. (Unchanged) The method of claim 16 wherein the bridges comprise multiple functional groups.

27. (Unchanged) The method of claim 16 wherein the treatment of the tissue further comprises exposing the tissue to activators.

28. (Unchanged) The method of claim 27 wherein the activators are selected from the group consisting of ultraviolet light, visible light and enzymes.

34. (Amended) A tissue comprising modified sites and bridge molecules, wherein said [the tissue is modified tissue and the] bridge molecules are bonded to two or more modified sites in the [modified] tissue.

35. (Unchanged) The tissue of claim 34 wherein the modified sites comprise aldehyde groups.

36. (Amended) A method of crosslinking tissue having modified sites comprising treating said [modified] tissue with a bridge composition comprising bridge molecules wherein the bridge[s] molecules bond to two or more modified sites in the [modified] tissue.

37. (Unchanged) The method of claim 36 wherein the modified sites comprises aldehyde groups.

38. (New) The tissue of claim 34 wherein said bridge molecules comprise functional groups selected from the group consisting of methylthio, amine, alcohol, carboxyl and combinations thereof.

39. (New) The tissue of claim 34 wherein said bridge molecules are substantially non-reactive to tissues having no modified sites.

40. (New) The tissue of claim 34 wherein said bridge molecules comprise functional groups located at opposite ends of said bridge molecules.

41. (New) The method of claim 36 wherein said bridge molecules comprise functional groups selected from the group consisting of methylthio, amine, alcohol, carboxyl and combinations thereof.

42. (New) The method of claim 36 wherein said bridge molecules comprise a functional groups located at opposite ends of said bridge molecules.

43. (New) The tissue of claim 1 wherein said bridge molecules are substantially non-reactive to tissues having no modified sites.